mandibuloacral dysplasia

Mandibuloacral dysplasia is a condition that causes a variety of abnormalities involving bone development, skin coloring (pigmentation), and fat distribution. People with this condition may grow slowly after birth. Most affected individuals are born with an underdeveloped lower jaw bone (mandible) and small collar bones (clavicles), leading to the characteristic features of a small chin and sloped shoulders. Other bone problems include loss of bone from the tips of the fingers (acroosteolysis), which causes bulbous finger tips; delayed closure of certain skull bones; and joint deformities (contractures).

People with mandibuloacral dysplasia can have mottled or patchy skin pigmentation or other skin abnormalities. Some people with this condition have features of premature aging (a condition called progeria), such as thin skin, loss of teeth, loss of hair, and a beaked nose. Some individuals with mandibuloacral dysplasia have metabolic problems, such as diabetes.

A common feature of mandibuloacral dysplasia is a lack of fatty tissue under the skin (lipodystrophy) in certain regions of the body. The two types of this disorder, mandibuloacral dysplasia with type A lipodystrophy (MADA) and mandibuloacral dysplasia with type B lipodystrophy (MADB) are distinguished by the pattern of fat distribution throughout the body. Type A is described as partial lipodystrophy; affected individuals have a loss of fatty tissue from the torso and limbs, but it may build up around the neck and shoulders. Type B is a generalized lipodystrophy, with loss of fatty tissue in the face, torso, and limbs.

MADA usually begins in adulthood, although children can be affected. MADB begins earlier, often just after birth. Many babies with MADB are born prematurely.

Frequency

Mandibuloacral dysplasia is a rare condition; its prevalence is unknown.

Genetic Changes

The two forms of mandibuloacral dysplasia are caused by mutations in different genes. Mutations in the *LMNA* gene cause MADA, and mutations in the *ZMPSTE24* gene cause MADB. Within cells, these genes are involved in maintaining the structure of the nucleus and may play a role in many cellular processes.

The *LMNA* gene provides instructions for making two related proteins, lamin A and lamin C. These proteins act as scaffolding (supporting) components of the nuclear envelope, which is the membrane that surrounds the nucleus in cells. The nuclear

envelope regulates the movement of molecules into and out of the nucleus and may help regulate the activity of certain genes. Mutations in this gene likely change the structure of lamin A and lamin C.

The lamin A protein (but not lamin C) must be processed within the cell before becoming part of the nuclear envelope. The protein produced from the *ZMPSTE24* gene is involved in this processing; it cuts the immature lamin A protein (prelamin A) at a particular location, forming mature lamin A. Mutations in the *ZMPSTE24* gene lead to a buildup of prelamin A and a shortage of the mature protein.

Mutations in the *LMNA* or *ZMPSTE24* gene likely disrupt the structure of the nuclear envelope. Researchers are working to understand how these genetic changes result in the signs and symptoms of mandibuloacral dysplasia.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- mandibuloacral dysostosis

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Mandibuloacral dysostosis
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0432291/
- Genetic Testing Registry: Mandibuloacral dysplasia with type B lipodystrophy
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1837756/

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Micrognathia
  https://medlineplus.gov/ency/article/003306.htm
- Encyclopedia: Progeria
  https://medlineplus.gov/ency/article/001657.htm
- Health Topic: Bone Diseases
  https://medlineplus.gov/bonediseases.html

Genetic and Rare Diseases Information Center

- Mandibuloacral dysplasia
  https://rarediseases.info.nih.gov/diseases/11893/mandibuloacral-dysplasia

Educational Resources

- Cedars-Sinai: Skeletal Dysplasia
  http://www.cedars-sinai.edu/Patients/Health-Conditions/Skeletal-Dysplasia.aspx
- Disease InfoSearch: Mandibuloacral dysostosis
  http://www.diseaseinfosearch.org/Mandibuloacral+dysostosis/8786
- Disease InfoSearch: Mandibuloacral dysplasia with type B lipodystrophy
  http://www.diseaseinfosearch.org/Mandibuloacral+dysplasia+with+type+B+lipodystrophy/4443
- MalaCards: mandibuloacral dysplasia
  http://www.malacards.org/card/mandibuloacral_dysplasia
- Orphanet: Mandibuloacral dysplasia
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=2457
- University of Texas Southwestern Medical Center: Lipodystrophy
  http://www.utsouthwestern.edu/education/medical-school/departments/internal-medicine/divisions/nutrition/lipodystrophy/

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/mandibuloacral-dysplasia/
- Progeria Research Foundation
  http://www.progeriaresearch.org/

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?term=%22mandibuloacral+dysplasia%22+%5BDISEASE%5D+OR+NCT00025883+%5BID-NUMBER%5D+OR+NCT00715546+%5BID-NUMBER%5D+OR+NCT00677313+%5BID-NUMBER%5D+OR+NCT00457938+%5BID-NUMBER%5D

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28mandibuloacral+dysplasia%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- MANDIBULOACRAL DYSPLASIA WITH TYPE A LIPODYSTROPHY
  http://omim.org/entry/248370
- MANDIBULOACRAL DYSPLASIA WITH TYPE B LIPODYSTROPHY
  http://omim.org/entry/608612

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